REMARKS

Status of Claims

Claims 1, 3-25 and 33-38 are pending. Claims 1, 17 and 18 have been amended. New claim 38 has been added. In view of cancellation of previous claims 26-32, it is respectfully submitted that no additional claim fee is required herein. Through this amendment, no new matter has been added. Support for this amendment, *inter alia*, can be found in paragraphs [0019], [0020], [0021] and [0056] of the subject application as published (US 2006/0251693).

Applicants' Response to 35 U.S.C. §102 Rejection over Short as evidenced by Alberts

Claims 1, 3-13, 15-16 and 36 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by WO Publication No. WO 01/31339 to Short et al. (hereinafter "Short") as evidenced by Molecular Biology of the Cell to Alberts et al. (hereinafter "Alberts").

The Examiner alleged that:

> Short teaches the steps, as part of said biological assay, in which a biological molecule is bound to a surface which has been treated by plasma polymerization. The step of 'binding' is reasonably interpreted as the biological molecule *contacting* the plasma treated surface. It is further the position of the Examiner, absent a showing of evidence to the contrary, that the newly added limitation of passively absorbed [sic] on the surface 'and thereby immobilized' recited in instant Claim 1, step v, is met by the disclosure of Short that the biological molecule is bound...the passively absorbed [sic] and thereby immobilized carbohydrate molecule retains its biological activity, is accorded no patentable weight as such an outcome would necessarily result from the method steps taught by Short which, as noted above, are the same as those recited in the instant Claim.

(Office Action of October 30, 2009, at pages 6-7) (citations omitted).

Claim 1 has been amended to further define the invention. In particular, a recitation has been added to claim 1 whereby the carbohydrate molecule remains in its native form. In addition, the plasma polymer coated surface is not modified prior to contacting the carbohydrate molecule to the plasma polymer coated surface. Support for this amendment can be found in

paragraphs [0019], [0020], [0021] and [0056] of the subject application as published.

Short discloses plasma polymerization of surfaces to which antagonists may bind and be assayed for use in the detection and/or activity of a biological molecule bound thereto. The purpose of the present invention is to obtain an immobilized surface that includes biologically active carbohydrates in their native form. As discussed at paragraphs [0055] and [0056] of the subject application as published,

> [0055] It is well known to those skilled in the art that the adsorption of specific polysaccharides, for example polysaccharides carrying a high net negative charge (e.g. sulphated GAGs e.g. heparin) to plastic surfaces is difficult to achieve. Plasticware which is available for biochemical and chemical assays (e.g. culture dishes, 96 well microtitre plates etc.) is typically manufactured from polystyrene (although it may be surface treated to improve binding properties). Surface treatments may include corona, plasma, acid or alkaline rinses, and flame. These treatments introduce a range of new surface functionalities into the plastic, mainly oxygen (alcohols, ethers, carbonyls and carboxyls, as well as peroxides). But, alone, these functionalities do not promote the passive adsorption of negatively charged molecules.
>
> [0056] In assays, it is preferred that the polysaccharide is adsorbed pure. Moreover it is preferred that the polysaccharide is not contaminated (e.g. with albumin or salts), or that the immobilization surface is modified (for example by the binding of a first biomolecule (for example, albumin) that will in turn bind the polysaccharide.

As set forth in claim 1, the subject invention provides an un-contaminated biologically active carbohydrate molecule in its native form adsorbed to a plasma polymer coated surface which is not modified. The combination of these elements provides a method and result not fully appreciated in Short.

It is respectfully submitted that claims 1, 3-13, 15-16, 36 and 38 are patentable over Short.

Applicants' Response to 35 U.S.C. §102 Rejection over Yan

Claims 1, 3, 5-7, 11, 18-20 and 22 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by U.S. Patent No. 6,776,792 to Yan et al. (hereinafter "Yan").

The Examiner alleged that:

> Yan et al. teach an implantable stent coated with a material that attracts the glycosaminoglycan carbohydrate heparin and forms a bond. Yan teaches that the stent surface coating is formed by plasma deposition with methane, ammonia gas, other amine containing monomers and acrylic acid. Yan also teaches contacting the plasma coated surface with heparin, via ionic bonds. Finally, Yan teaches the incubation step recited in amended Claim 1 by pretreating the plasma coated surface (stent) with a heparinized saline solution prior to implantation in order to adjust the heparin level. Therefore, the carbohydrate is immobilized using the method steps recited in instant Claim 1 and accordingly, such an outcome results in heparin being passively (ionically) absorbed and retaining its anticoagulant biological activity.

(Office Action, at page 9) (citations omitted)

Yan is directed to a coated endovascular stent. The stent is coated with a material that attracts heparin, so that heparin thus forms a bond with the material. (See, e.g., col. 2, ll. 57-60). The purpose of Yan is to prepare a stent that is biocompatible upon implantation. Yan includes a coating with functional groups that attract heparin. Yan describes a plasma deposition as a possible embodiment to obtain the coating. The steps for the plasma deposition include depositing a base or primer layer to "prepare the surface of the stent to receive the functionality group containing substance" (Yan, col. 3, ll. 4-5) and a second or "top layer that includes the desired functionalities" (Yan, col. 3, ll. 9-10).

As set forth in claim 1, "the carbohydrate molecule is passively adsorbed on the surface and thereby immobilised". The bonding in Yan is not immobilization. Yan indicates that "a heparin molecule [may] become detached" (col. 3, l. 67) and that the heparin may need to be "replenished" (col. 4, ll. 9-12). As discussed at paragraph [0051] of the subject application as

published, the immobilized molecule is one which "cannot be desorbed by washing, or by the typical processes carried out in biochemical or chemical assays." Yan provides bonding, but not immobilization.

It is respectfully submitted that claims 1, 3, 5-7, 11, 18-20 and 22 are patentable over Yan.

Applicants' Response to 35 U.S.C. §103 Rejection over Short as evidenced by Alberts and Karwoski

Claims 14 and 33-34 were rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Short as evidenced by Alberts and further in view of U.S. Patent No. 4,632,842 to Karwoski et al. (hereinafter "Karwoski").

As stated in detail above, Short fails to disclose each and every element of claim 1, as amended herein. Karwoski was merely cited for its disclosure of the formula W/FM. Nowhere in Karwoski is it disclosed or suggested to utilize a carbohydrate in its native form or a polymerized surface that has not been modified prior to contact with the carbohydrate in its native form. Accordingly, Karwoski fails to cure the deficiencies of Short. It is respectfully submitted that claims 14 and 33-34 are patentable over Short, Alberts and Karwoski, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Yan, and further in view of Mori

Claim 17 was rejected under 35. U.S.C. §103(a) as being allegedly unpatentable over Yan in view of U.S. Patent No. 5,053,398 to Mori et al. (hereinafter "Mori").

As stated in detail above, Yan fails to disclose each and every element of claim 1, as amended herein. Mori discloses sulfated homopolysaccharides with anti-HIV activity.

However, Mori does not disclose or suggest immobilization of such homopolysaccharides, and, as such, Mori fails to overcome all the deficiencies of Yan in this regard. It is respectfully submitted that claim 17 is patentable over Yan and Mori, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Short as evidenced by Alberts and Nomura

Claim 35 was rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Short as evidenced by Alberts and further in view of U.S. Patent No. 6,022,602 to Nomura et al. (hereinafter "Nomura").

As stated in detail above, Short fails to disclose each and every element of claim 1, as amended herein. Nomura is directed to a lumen surface of tubing that has been modified with plasma. Nomura was merely cited for its disclosure of an alkane. Accordingly, Nomura fails to cure the deficiencies of Short. It is respectfully submitted that claim 35 is patentable over Short, Alberts and Nomura, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Short, and further in view of Nilsson

Claim 21 was rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Short and further in view of U.S. Publication No. 2001/0017270 to Nilsson et al. (hereinafter "Nilsson").

As stated in detail above, Short fails to disclose each and every element of claim 1, as amended herein. Nilsson refers to a biosensor in which a carbohydrate or a derivative thereof is bound to a surface of the biosensor *via* a chemical bond or adsorption. In particular, Nilsson states "the surface of the biosensor can be, for example a gold surface or a modified gold surface, a plastic surface which has been modified with a gold surface, silver surface or another metallic

surface, or modifications thereof with polymers to which **chemical coupling** of carbohydrate can be carried out." (See Nilsson, page 3, paragraph [0041], emphasis added). However, nowhere does Nilsson describe any modifications to a plasma polymer surface for passive adsorption of a carbohydrate. Likewise, nowhere does Nilsson exemplify a biosensor with a polymer surface. Rather, Nilsson exemplifies the following:

a) binding of digalactoside with aglycon (*i.e.*, Galα1-4Galβ-OEtSEtCONHNH$_2$) to a silica surface coated with a gold layer modified with mercaptopropionic acid

b) binding of Galα1-4GalβOCH$_2$CH$_2$SCH$_2$C(O)-NHNH -BSA to a silica surface coated with a gold layer modified with mercaptopropionic acid

c) binding of Galα1-4Galβ-BSA to a silica surface coated with a gold layer (not pretreated with mercaptopropionic acid)

Thus, Nilsson teaches biosensors with a surface coated with a gold layer. Nowhere in Nilsson is it disclosed or suggested to provide a plasma polymerized surface that is not modified prior to coming into contact with a carbohydrate. Moreover, nowhere in Nilsson is utilizing a carbohydrate in its native form disclosed or suggested. Accordingly, Nilsson does not overcome the deficiencies noted above of Short. It is respectfully submitted that claim 21 is patentable over Short, Alberts and Nilsson, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Yan, and further in view of Earhart

Claim 23 was rejected under 35. U.S.C. §103(a) as being allegedly unpatentable over Yan in view of U.S. Patent No. 6,077,232 to Earhart et al. (hereinafter "Earhart").

As stated in detail above, Yan fails to disclose each and every element of claim 1, as amended herein. Earhart teaches a blood collection device containing an anticoagulant composition. Specifically, Earhart states that,

> The anticoagulant composition is a **soluvated** non-aqueous **solution** comprising a proteinase inhibitor such as for example but not limited to a polysaccharide sulfuric acid ester such as for example heparin. The composition also comprises a blend of one or more alcohols such as for example one or more polyhydric alcohols selected from the group consisting of C1-12 diols such as glycols and derivatives thereof such as for example ethylene glycol or propylene glycol wherein ethylene glycol is preferred for increased solubility and C1-12 polyalkyl diols such as for example polyethylene glycol, polyproplylene glycol or polybutylene glycol wherein polyethylene glycol is preferred for increased solubility and for ready plasticization of the proteinase inhibitor.
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> (col. 2, l. 62 – col. 3, l.8).

Furthermore, Earhart states that "the subject anticoagulant composition is placed within the syringe barrel in a liquid state...and remains in the syringe barrel during blood collection due to its movement within the barrel without expulsion thereof." (col. 1, l. 62 to col. 2, l. 6). Thus, the anticoagulant composition is not immobilized to the surface but rather in a liquid state that freely moves. In fact, Earhart further emphasizes that, "The alcohol which is preferably polyethylene glycol, combined with the proteinase inhibitor which is preferably heparin, prevents the proteinase inhibitor from drying into an unsoluvated state. Heparin in an unsoluvated state dissolves with difficulty and thus requires more time to disperse throughout a collected blood sample." (col. 2, ll. 15-21). In fact, Earhart points out that "the use of the anticoagulant composition of the present invention within a blood collection device reduces the anticoagulant solution dispersal time compared to that of dried unsoluvated heparin within a blood collection device so as to be more effective in preventing coagulation within a collected blood sample." Thus, the proteinase inhibitor, heparin, is preferably a liquid which disperses readily throughout a blood sample collected in the blood collection device. Nowhere does Earhart disclose or suggest immobilizing heparin.

Without immobilization, it is respectfully submitted that Earhart does not overcome the deficiencies noted above of Yan. It is respectfully submitted that claim 23 is patentable over Yan and Earhart, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Short, and further in view of Brigstock

Claim 24 was rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Short and further in view of U.S. Publication No. 2001/0007019 to Brigstock et al. (hereinafter "Brigstock").

As stated in detail above, Short fails to disclose each and every element of claim 1, as amended herein. Brigstock teaches heparin-binding growth factor (HBGF) polypeptides as well as nucleic acids encoding the same and antibodies which bind to the HBGF polypeptides. Brigstock discloses the use of a heparin affinity chromatographic column in its purification of HBGF polypeptides. (page 7, paragraphs [0060] to [0063]). However, no additional detail regarding such a heparin affinity chromatographic column is provided. With no details on whether or not the polypeptides are immobilized, Brigstock does not overcome the deficiencies noted above of Short. It is respectfully submitted that claim 24 is patentable over Short and Brigstock, each taken alone or in combination.

Applicants' Response to 35 U.S.C. §103 Rejection over Short, and further in view of Dukler

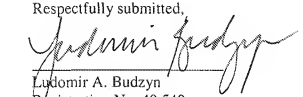
Claim 25 was rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Short and further in view of U.S. Publication No. 2002/0094541 to Dukler et al. (hereinafter "Dukler").

As stated in detail above, Short fails to disclose each and every element of claim 1, as amended herein. Dukler was cited for its alleged disclosure of a microarray. Dukler teaches combinatorial complex libraries and methods for the manufacture of addressable complex carbohydrate microarrays as well as uses thereof. As the carbohydrate microarrays of Dukler are addressable, one of skill in the art would not be motivated to employ passive adsorption of carbohydrates to the substrate surface since such non-covalent bonds would be impractical to

produce in an addressable format. Dukler states that, "the libraries according to the present invention are preferably synthesized on a solid phase support. As such, the first building block is provided with a suitable functional group for binding such a support." (page 15, paragraph [0165]). Furthermore, with respect to linking the first saccharide building block to the solid phase support, Dukler states, "The first saccharide building block is preferably covalently attached to the solid phase matrix via a single atom (e.g., the solid phase functional group) or a linker." (page 15, paragraph [0154]). In fact, Dukler states, "... covalent immobilization methods enable the use of a very high ionic strength buffer (e.g., 6 M Guanidine HCl or 100 mM NaOH) in subsequent washing steps thus allowing accurate "in situ" verification of each enzymatic step utilized by the process. The removal of nonspecifically bound molecules is crucial for accurate library synthesis." (page 49, paragraph [0242] and [0243], first sentence). Thus, one of skill in the art reading Dukler would choose covalent attachment over non-covalent attachment of a carbohydrate to a surface of the microarray. Nowhere in Dukler is it disclosed or suggested to utilize a carbohydrate in its native form or a polymerized surface that has not been modified prior to contact with the carbohydrate in its native form. Accordingly, Dukler does not overcome the deficiencies noted above of Short. It is respectfully submitted that claim 25 is patentable over Short and Dukler, each taken alone or in combination.

Favorable action is earnestly solicited. If there are any questions or if additional information is required, the Examiner is respectfully requested to contact Applicants' attorney at the number listed below.

Respectfully submitted,



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